REMARKS

Applicant thanks the Examiner for withdrawing the objections to the specification and some of the rejections under 35 U.S.C. §§ 101, 112 and 102 in view of Applicant's previous Amendment and Response. In this Response After Final Rejection, Applicant further clarifies information presented in support of patentability of the claims. Claims 1-7, 12 and 23-25 are pending.

Rejection of Claims 1-7, 12 and 23-25 Under 35 U.S.C. §101

The rejection of claims 1-7, 12 and 23-25 under 35 U.S.C. §101 was maintained because the Examiner does not believe that the expression results cited by Applicant are specific to the claimed polynucleotide. The Examiner contends that the expression does not depend on any characteristics of the nucleic acid molecule itself and that further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. The Examiner further alleges that the specification does not teach whether the tumor tissue cited for expression results was malignant or benign and believes it important to know whether cell lines or biopsies were used. The Examiner further takes issue with the statements of relative levels of expression (high, medium or low) as providing insufficient data to enable one of skill in the art to diagnose any particular cancer. The Examiner is not convinced by Applicant's arguments of the specificity of the gene expression studies for the 25466 nucleic acid structure and real world use of the expression results described in the Specification. Applicant respectfully traverses this rejection by further clarifying these points for the Examiner.

Applicant is submitting herewith a Declaration Under 37 C.F.R. §1.132 by Sunita Badola, who performed for the Applicant the gene expression analysis described in the specification at paragraphs [00366] – [00370]. Ms. Badola's Declaration provides further information to clarify the points held at issue by the Examiner and explains how the results of this analysis can be carried over to real world uses. In particular, the Declaration identifies, in paragraph 4, the sequences in the 25466 nucleic acid molecule used to identify the expression of 25466; clarifies, in paragraph 5, the sources and degree of malignancy of the tumor tissue samples used in the analysis; and explains, in paragraph 6, how statements of level of expression of genes determined by analysis of Taqman® quantitative Real Time PCR results provides the skilled practitioner with real world diagnostic information on tumor presence for certain tissues.

As can be seen by Ms. Badola's Declaration, the gene expression analysis quantified the presence of 25466 by amplifying a portion of the open reading frame of the 25466 transcript. In addition, the tumor samples were from malignant tumors and not from benign tumors or cell lines. Furthermore, the terms described for the amount of expression as interpreted from the numerical results reflect levels which have real world use for predicting tumors in ovary, lung and colon. Applicant believes that this

information clarifies the issues held by the Examiner. Together with the previous arguments that the ability to detect the presence of a cellular proliferative and/or differentiative disorder imparts upon the 25466 molecules of the invention a credible, specific, substantial and well-established utility, Applicant respectfully asks that this rejection be withdrawn.

Rejection of Claims Under 35 U.S.C. §112, First Paragraph

The rejection of claims 1-7, 12, 23 and 24 under 35 U.S.C. §112, first paragraph was maintained because of the contention that if the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention. Applicant respectfully traverses the rejection. The response to the previous utility rejection, supplemented with the clarifying information in the Declaration Under 37 C.F.R. §1.132 by Sunita Badola and the present remarks in response to the maintained utility rejection shows that there is a specific or substantial asserted utility or a well-established utility for the molecules of the invention. In particular, the claimed molecules have utility in diagnosis of a cellular proliferative and/or differentiative disorder. The present application provides support to enable one skilled in the art to use the molecules for this purpose at, for example paragraphs [00255]-[00282]. In view of the remarks, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1, 3-7, 12, 23 and 24 under 35 U.S.C. §112, first paragraph was maintained on the grounds that the specification does not contain a written description of the claimed invention and does not convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

Specifically, the Examiner contends that Applicant provides no information as to the structures of the allelic variants or the fragments of nucleic acid molecules. The Examiner further remarks that one cannot recognize an allelic variant until the protein is expressed and the activity is assayed. By reference to the previous office action, the Examiner states that the claimed genus encompasses hundreds of thousands of different nucleic acid molecules encoding polypeptides with varying structures and functions and that there is no guidance in the art as to what the defining characteristics of a 25466 polypeptide might be. The Examiner maintains that there are no identifying characteristics of the nucleic acid molecules such that one of skill would be able to predictably identify the encompassed molecules and cannot envision their detailed chemical structure. Applicant respectfully traverses this rejection for the following reasons.

First of all, the only fragment embodiment in the present claims is recited in claim 1d). This embodiment recites a fragment consisting of a domain identified by its sequence. Certainly that structure

is defined sufficiently for someone skilled in the art to immediately recognize its structure. In case any question remains regarding this fragment's recognizability, Applicant has further recited the function of the encoded polypeptide in the claim to allow confirmation of the structure encompassed by the claim.

Claims 1c) (claims 3-7, 23 and 24 dependent thereon) and 12 are drawn to a nucleic acid containing a nucleotide sequence which: (a) hybridizes to a reference polynucleotide sequence under defined conditions of hybridization and washing; and (b) encodes a polypeptide which binds a monocarboxylated ion. The specification at pagagraph [0068] describes the hybridization conditions recited in the claims as "very high stringency," i.e. more stringent than all the other conditions taught in that paragraph. This comment is due to requirement of performing both the hybridization and the wash at high temperature (65°C) and performing the wash at low salt (0.2X SSC). In particular, under these conditions, significantly mismatched nucleic acids will either not hybridize to the reference nucleic acid, or will be washed away during the washing step. Enclosed as Exhibits C1 and C2 are portions of Unit 2.10 and Unit 6.3, respectively, of *Current Protocols of Molecular Biology*, which describe the influences of hybridization and washing conditions on the ability to detect the hybridization of non-homologous sequences to blots. In these Units, the ability of nucleic acid molecules to hybridize to each other as temperature is raised requires progressively less mismatch between their nucleotide sequences (see page 2.10.8 and table 2.10.2). The ability to remain hybridized during washing is diminished as mismatch increases, temperature increases and washing salt concentration decreases (see page 6.3.6). As a result of these very high stringency hybridization and washing conditions, only nucleic acids very highly related to the recited polynucleotide sequence will hybridize and remain hybridized following the hybridization and washing steps specified in the claims.

The genus of nucleic acids encompassed by claims 1c) (claims 3-7, 23 and 24 dependent thereon) and 12 does not have substantial variation, since each nucleic acid must encode a polypeptide that has a specified activity (i.e. the ability to bind a monocarboxylated ion) and contain a structurally similar nucleotide sequence to the sequence recited in the claims (i.e., one that hybridizes to the reference sequence under the hybridization and washing conditions recited in the claims). The 25466 nucleic acids disclosed in the specification are representative of the claimed genus because all members of the genus hybridize under very high stringency to a 25466 nucleic acid. The position by the Examiner on this point is contrary to the position in the Written Description Guidelines, Example 9. In Example 9, given the actual reduction to practice of the reference sequence and the conventional nature of the techniques for hybridizing DNA under highly stringent conditions,

> "a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in

combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention."

This position in the Written Description Guidelines is taken even without the added claim limitation of required function by the polypeptide encoded by the nucleic acid molecule encompassed by the claim."

Additional distinguishing characteristics of the encompassed nucleic acids are included in the specification. For example, a nucleic acid structurally similar to SEQ ID NO:1 will have approximately the same size open reading frame as identified for SEQ ID NO:1 in paragraph [0023] and will encode a polypeptide structurally similar to SEQ ID NO:2, whose complete sequence is described. As described in paragraph [0037], a polypeptide structurally similar to SEQ ID NO:2 will have transmembrane domains and will bind the monocarboxylated ion in non-transmembrane regions. Such a polypeptide should have the consensus sequences described in paragraph [0037]. Such a polypeptide should have an MCT domain as described in paragraph [0038] and similar spacing and orientation of the non-transmembrane regions as described for 25466 in paragraph [0043]. Other features of a polypeptide with high similarity to 25466 of SEQ ID NO:2 can be found in other paragraphs from [0025] to [0048]. All these features are discernable just by knowing the nucleic acid molecule and being able to locate and translate an open reading frame in a nucleic acid sequence, both capabilities within the level of skill in the art. Additionally, one skilled in the art would be able to judge by the nucleotide sequence differences of the nucleic acid in question and SEQ ID NO:1 and corresponding encoded polypeptide sequence differences from SEQ ID NO:2 whether a nucleic acid would encode a polypeptide with the activity recited in the claim. For example, in paragraph [0073], the specification defines a conservative amino acid substitution likely not to affect activity of the polypeptide and the desirability of modifying only non-essential amino acids, as defined in paragraph [0072]. Therefore, the specification provides structural information to determine whether a variant nucleic acid molecule would be encompassed by the claim and would not necessarily need to express a protein and assay its activity.

The remarks above clarify how one of skill in the art would know from the hybridization conditions and the structural information provided in the specification that the reference sequence provided by the Applicant shows possession of the scope of the invention encompassed by the pending claims. In view of these remarks, Applicant maintains that possession of the invention at the time of filing the application was demonstrated to one skilled in the art and respectfully requests that this rejection be withdrawn.

CONCLUSIONS

Applicant respectfully requests that the Examiner consider these remarks after final rejection because, in view of these remarks, Applicant respectfully submits that the rejections of claims 1-7, 12 and

23-25 under 35 U.S.C. §§ 101 and 112 are herein overcome and that this application is now in condition for allowance. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the allowance of the subject application, the Examiner is encouraged to call the undersigned. If the Examiner disapproves of Applicants' remarks in this response, Applicants request a prompt mailing of an Advisory Action to that effect.

This paper is being filed timely within two months of the mailing date of the final action. No extensions of time are required. In the event any extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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